

Carcinoma of the Oral Cavity

An Analysis of 478 Cases

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Evaluation and analysis of 478 cases of carcinoma of the oral cavity treated from 1947 through 1970 shows a significant improvement in radiotherapy in the supervoltage (Co_{60}) era. Survival in the early stages of disease (I and II) improved in the supervoltage era but not in the later stages of disease (III and IV). Results with combined therapy for advanced disease showed no significant difference from that of single mode therapy, whether with radiotherapy or with surgery in the supervoltage era.

TUMOR REGISTRIES, which were instituted within the Army's medical system by 1947, have facilitated the accrual and close followup of cancer patients treated in our military hospitals. These registries have permitted us to evaluate a large number of cases of carcinoma of the oral cavity treated at Walter Reed, Brooke, and Fitzsimons Army Medical Centers over the period 1947 through 1970. This is a review of our experience with the

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treatment of carcinoma of the oral cavity at these three centers.

Methodology

Over 500 cases of carcinoma of the oral cavity were registered in the period 1947 through 1970. These were reviewed. Four hundred seventy eight cases met the criteria of having had definitive care or initial evaluation and followup when treatment was either palliative or refused. All sites of the oral cavity (except lip) are included (Table 1).

The T N M classification and staging is that provided by the American Joint Committee (AJC) for cancer and end results reporting, February 1968.²

Figure 1 shows the distribution of those cases treated definitively. The numbers of cases (per cent) show a relatively even distribution among Stages I, II, and III, the three major stages to be considered.

The direct method as described by MacDonald¹⁰ and Berkson and Gage¹ is used for calculating determinate survival.

The Chi square method was used to determine statistical significance.⁹

In determining control of disease, those patients for whom followup was available for at least two years and who had no evidence of disease (NED) were considered controlled because in our experience, and in the experience of others,^{3,14} 85% to 95% of recurrences occur within two years after treatment. The designation "control" in this review means *control of the treated area*. For example, those patients with Stages III and IV le-

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TABLE 1. Carcinoma of the oral cavity (1947-1970): distribution.

	NO.	%
FLOOR OF MOUTH	155	33
ANTERIOR 2/3 TONGUE	129	27
POSTERIOR 1/3 TONGUE	63	13
PALATE	59	12
ALVEOLAR RIDGE	58	12
BUCCAL MUCOSA	14	3
Total	478	100

sions were treated for the primary site and the neck disease. Patients with recurrence in the primary site or the neck were considered *not controlled* (failures of treatment). In a majority of Stage I lesions, treatment was given to the primary site only. Patients with recurrence at the primary site are considered as failures of treatment. Patients who later manifest disease in the neck (with no prior treatment to the neck) are not considered as failures of treatment. In Stage II lesions, many of the larger lesions were treated at both the primary site and the neck. Any treatment failure in this category would mean recurrence at either the primary site or the neck.

Two treatment periods are considered: 1) 1947-1963 (orthovoltage era) and 2) 1964-1970 (supervoltage era) when Co_{60} radiotherapy became more widely used at all three centers, although available earlier.

For analysis, only those cases treated by surgery, radiotherapy, or combined therapy (radiotherapy/surgery) are considered. A few cases received palliative therapy only (radiotherapy and/or chemotherapy) or no treatment (Table 2).

Figure 2 shows the distribution of the modes of therapy used for the cases considered for analysis. In this series, radiotherapy was used more often than the other two modes combined.

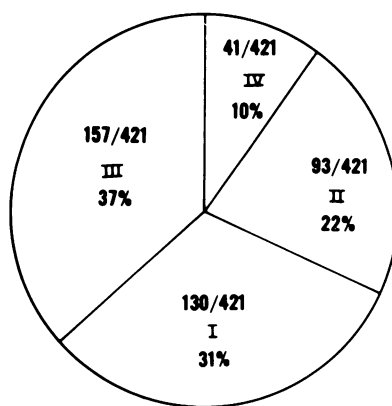


FIG. 1. Note the even distribution of cases by stage.

TABLE 2. Mode of Therapy

Radiotherapy	250
Surgery	112
Radiotherapy-Surgery	100
Palliative Therapy	11
Chemotherapy	2
No Therapy	3
Total	478

Clinical Data

Selection of Treatment

The multidiscipline approach to treatment has been in effect from the outset. Patients and their problems are discussed in conference with staff representation from General Surgery, Otolaryngology, Plastic Surgery, Radiotherapy, Oral Surgery, and Medical Oncology. Each case has been handled individually with no formal protocol of treatment. The ultimate decision on mode of treatment rests with the clinical service which has primary care of the patient. At Walter Reed Army Medical Center, the creation of the Head and Neck Surgery Service in 1964 placed primary responsibility for treatment of head and neck cancer with that service. At Fitzsimons Army Medical Center and at Brooke Army Medical Center, there is no formal Head and Neck Surgery Service.

In the orthovoltage era, the 250 KV Unit provided external radiotherapy. The treatment doses ranged from 2000r-6000r, depending on the patient's ability to tolerate the therapy. Many patients received radium implant therapy with or without external therapy. Heavy reliance was placed on radium implants to provide tumor doses in ranges of 6000r to 8000r and occasionally higher.

In the supervoltage era, preoperative radiotherapy ranged from 3000r to 5000r at 200r daily dose (1000r/wk) and full radiotherapeutic dose generally ranged from 6000r to 7000r.

In general, wide excision of the primary was the surgical procedure for small lesions, while the larger primary

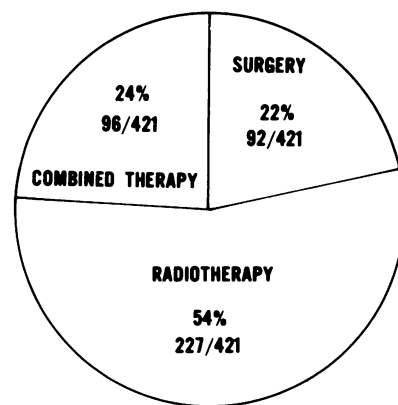


FIG. 2. The preponderance of cases treated by radiotherapy.

TABLE 3. Overall primary control: Control refers to control of the treated area.

	1947-1963	1964-1970	1947-1970
RADIOTHERAPY	39% ($\frac{57}{145}$)	52% ($\frac{47}{88}$)	45% ($\frac{104}{233}$)
SURGERY	79% ($\frac{45}{57}$)	76% ($\frac{29}{38}$)	78% ($\frac{74}{95}$)
COMBINED THERAPY	62% ($\frac{34}{54}$)	57% ($\frac{24}{42}$)	60% ($\frac{58}{96}$)
			56% ($\frac{236}{424}$)

lesion and those with clinically positive nodes received composite procedures (resection of the primary with separate or incontinuity radical neck dissection).

Primary Control

The overall control rates for each mode of therapy are listed in Table 3. Better results were obtained with surgery and with combined therapy than with radiotherapy over the entire period. The control rate by surgery was the best. This was due, in part, to a better selection of cases. Of great interest is the significant improvement of radiotherapy in the supervoltage era ($0.01 < P < 0.05$) while surgery or combined therapy showed no significant improvement in control between the two periods of study.

In our series of cases, analysis of control of disease and survival rates by sites of the lesions and stages of the disease showed no significant difference in the results between sites for the comparable stages of disease. Therefore, sites of the oral cavity are combined for each stage of disease for further analysis of control of disease and for the three year survival comparisons.

Table 4 shows control of disease for each mode of therapy. This reveals the mediocre results of

radiotherapy in the orthovoltage era, particularly in Stages I and II. In the supervoltage era, there is significant improvement in radiotherapy for these stages ($0.01 < P < 0.05$), while there is no significant improvement in results by surgery or combined therapy. There was also some improvement in radiotherapy for Stage III lesions (not statistically significant). Examination of our results in the supervoltage era shows no significant difference among the three modes of therapy for each stage of disease.

Analysis of control of disease by size and extent of the lesion (Table 5) for the entire period of study reveals the expected progressive decrease in control rates as the size of the lesion and the extent of disease increases. However, in this series, a breakdown of Stage III shows that for the T_1N_1 lesion, the control rate is significantly better than that of any other category in Stage III ($0.01 < P < 0.05$) and is equivalent to that of a Stage II lesion (no statistical difference).

Failures

There were considerably more failures by radiotherapy than by surgery or combined therapy (Table 6). This is, in large part, due to poorer therapy in the orthovoltage era and to a greater number of larger lesions treated by radiotherapy than by surgery or combined therapy. Salvage attempts could be made on approximately one-half of the failures of radiotherapy or surgery and were successful in one-sixth of all failures (one third of attempts). On the other hand, very few attempts could be made for patients treated with combined therapy (4/37), and only one was salvaged.

Survival

Table 7 compares our determinate 5-year survival rates with those reported by the American Joint Committee in

	I		II		III		IV	
	A*	B*	A	B	A	B	A	B
RADIOTHERAPY	60 ($\frac{32}{53}$)	83 ($\frac{20}{24}$)	38 ($\frac{10}{26}$)	73 ($\frac{16}{22}$)	29 ($\frac{15}{52}$)	41 ($\frac{11}{27}$)	($\frac{0}{14}$)	($\frac{0}{15}$)
SURGERY	96 ($\frac{25}{26}$)	95 ($\frac{20}{21}$)	67 ($\frac{8}{12}$)	75 ($\frac{6}{8}$)	65 ($\frac{11}{17}$)	43 ($\frac{3}{7}$)	($\frac{0}{2}$)	($\frac{1}{2}$)
COMBINED THERAPY	($\frac{2}{3}$)	($\frac{3}{3}$)	85 ($\frac{11}{13}$)	75 ($\frac{9}{12}$)	53 ($\frac{17}{32}$)	50 ($\frac{10}{20}$)	67 ($\frac{4}{6}$)	($\frac{0}{4}$)
OVERALL	73 ($\frac{59}{81}$)	88 ($\frac{43}{48}$)	57 ($\frac{29}{51}$)	74 ($\frac{31}{42}$)	43 ($\frac{43}{101}$)	44 ($\frac{24}{54}$)	18 ($\frac{4}{22}$)	5 ($\frac{1}{21}$)

*A = 1947-1963

*B = 1964-1970

TABLE 4. Per cent primary control by staging: Control refers to control of the treated area.

TABLE 5. Control by size and extent of disease (1947-1970).

MODE OF THERAPY	T ₁ N ₀	T ₂ N ₀	T ₃ N ₀	T ₁ N ₁	T ₂ N ₁	T ₃ N ₁	IV
RADIOTHERAPY	67% ($\frac{52}{77}$)	54% ($\frac{26}{48}$)	37% ($\frac{7}{19}$)	50% ($\frac{7}{14}$)	30% ($\frac{7}{23}$)	22% ($\frac{4}{18}$)	($\frac{0}{28}$)
SURGERY	96% ($\frac{45}{47}$)	70% ($\frac{14}{10}$)	50% ($\frac{2}{4}$)	91% ($\frac{10}{11}$)	50% ($\frac{3}{6}$)	17% ($\frac{1}{6}$)	25% ($\frac{1}{4}$)
RAD/SURG	83% ($\frac{5}{6}$)	80% ($\frac{20}{25}$)	38% ($\frac{3}{8}$)	80% ($\frac{4}{5}$)	56% ($\frac{15}{27}$)	50% ($\frac{8}{16}$)	44% ($\frac{4}{9}$)
OVERALL	79% ($\frac{102}{130}$)	65% ($\frac{60}{93}$)	39% ($\frac{12}{31}$)	70% ($\frac{21}{30}$)	45% ($\frac{25}{56}$)	33% ($\frac{13}{40}$)	12% ($\frac{5}{41}$)

February 1968. As stated earlier, in our series, there is no significant difference in survival among the sites for the same stage of disease. Therefore, our overall 5 year survival by stage is also shown. The overall 5-year survival for the entire series is 57%.

Finally, Table 8 shows the comparison of determinate 3-year survival rates between the orthovoltage and supervoltage eras. There is improvement in survival for Stage I (not statistically significant) and Stage II disease (statistically significant, $(0.01 < P < 0.05)$). There was no improvement in survival for Stages III and IV.

Complications

Complications of treatment have not been analyzed for this review. A casual screening of our cases revealed frequent osteoradionecrosis and/or persistent ulcer after radiotherapy in the orthovoltage era. In the supervoltage era, these complications were infrequent.

Multiple Primaries

There was a 13% incidence of multiple primaries in 478 patients studied. These include other primary cancers which occurred before, simultaneous with, or after discovery of the oral carcinoma. This incidence is somewhat higher than that reported by Marchetta.¹¹

TABLE 6. Failures.

MODE OF THERAPY	FAILURES	SALVAGE ATTEMPTS	SALVAGES
RADIOTHERAPY	124	$\begin{array}{l} \text{R} \quad 14 \\ 61 \begin{array}{l} \text{S} \quad 41 \\ \text{R/S} \quad 6 \end{array} \end{array}$	$\begin{array}{l} 3 \\ 21 \begin{array}{l} 17 \\ 1 \end{array} \end{array}$
SURGERY	22	$\begin{array}{l} \text{R} \quad 6 \\ 14 \begin{array}{l} \text{S} \quad 3 \\ \text{R/S} \quad 5 \end{array} \end{array}$	$\begin{array}{l} 0 \\ 3 \begin{array}{l} 2 \\ 1 \end{array} \end{array}$
RAD/SURG	37	$\begin{array}{l} \text{R} \quad 1 \\ 4 \begin{array}{l} \text{S} \quad 2 \\ \text{R/S} \quad 1 \end{array} \end{array}$	$\begin{array}{l} 0 \\ 1 \begin{array}{l} 1 \\ 0 \end{array} \end{array}$
	183	79	25

Comments

Radiotherapy was noticeably inferior to surgery or combined therapy in the orthovoltage era. Results like these in our series which showed the superiority of surgery probably led oncologic surgeons like Martin⁵ to become discouraged with radiotherapy and to relegate it to an adjuvant role. The inferiority is particularly noticeable for lesions of Stages I and II. With the advent of the supervoltage era, radiotherapy has improved considerably, such that in each stage of disease, control of disease is equivalent to those of surgery and combined therapy, in our series. Our results in the supervoltage era agree with those of some surgeons⁵ and most radiotherapists who report or claim equivalent results, at least for Stages I and II.

Surgery has provided excellent control rates in our series, particularly in Stages I and II. There is also a tendency towards acceptable and reasonable control and survival rates in Stage III disease. However, surgery was only used to a limited degree for treatment of Stage III lesions. Figure 3 compares, as an overall view, the percentage of cases treated by each mode of therapy and the control rates obtained for each stage of disease. It would have been of more than passing interest to treat more cases in Stage III with surgery to provide a better comparison of results with radiotherapy.

Patients treated by a single mode of therapy (surgery or radiotherapy) had a 17% chance of salvage if there was failure of treatment, while those patients treated by combined therapy had virtually no chance of salvage (1/37). There would appear to be little justification in using combined therapy for lesions in Stages I and II because of the excellent control rates by single mode therapy with no apparent improvement with combined therapy. This also provides for keeping a major mode of therapy in reserve for failures of treatment with a better chance for salvage.

There was no improvement in the control of disease or of survival in Stages III and IV in the supervoltage era. This has been disturbing because, 1) there was significant improvement in radiotherapy, and, 2) no deterioration in the quality of surgery. There was also improvement in

FIVE YEAR SURVIVAL

1947 - 1970

SITE	STAGE I		STAGE II		STAGE III		STAGE IV	
	MIL	AJC	MIL	AJC	MIL	AJC	MIL	AJC
FLOOR OF MOUTH	84%	68%	63%	70%	38%	50%	$(\frac{2}{11})$	9%
ANTERIOR 2/3 TONGUE	79%	90%	72%	64%	45%	34%	$(\frac{1}{8})$	6%
POSTERIOR 1/3 TONGUE	$(\frac{1}{1})$	$(\frac{2}{4})$	$(\frac{2}{3})$	44%	41%	26%	$(\frac{0}{15})$	0.7%
PALATE	$(\frac{4}{4})$	83%	$(\frac{5}{7})$	44%	62%	24%	$(\frac{0}{4})$	6%
ALVEOLAR RIDGE	$(\frac{6}{7})$	63%	$(\frac{3}{8})$	56%	40%	36%	$(\frac{0}{2})$	17%
BUCCAL MUCOSA	$(\frac{1}{1})$	72%	$(\frac{2}{2})$	61%	$(\frac{4}{7})$	42%		0
OVERALL	83%		68%		45%		7.5%	

TABLE 7. Five-year survival (1947-1970).

TOTAL 57% $(\frac{176}{309})$

radiotherapy of Stage III lesions. It would then appear logical to expect improvement with combined therapy. Yet there was no improvement in survival with combined therapy. Earlier in this review, we indicated that there was also no improvement in control of disease by combined therapy for Stage II disease. Our results are, therefore, at variance with those who have recently reported improvement with combined therapy for advanced disease,^{4,7,8,14} and are more consistent with those who remain cautious on the efficacy of combined therapy for advanced disease.^{6,12,13} It would appear that, at this time, the only sure way of increasing overall survival is to discover lesions early in the natural history and treat accordingly.

TABLE 8. Staged 3-year survival.

	1947-1963	1964-1970	1947-1970
Stage I	87% $(\frac{71}{82})$	96% $(\frac{44}{46})$	90% $(\frac{115}{128})$
Stage II	69% $(\frac{40}{58})$	90% $(\frac{35}{39})$	78% $(\frac{75}{97})$
Stage III	57% $(\frac{62}{108})$	59% $(\frac{29}{49})$	58% $(\frac{91}{157})$
Stage IV	15% $(\frac{3}{20})$	19% $(\frac{4}{21})$	18% $(\frac{7}{41})$
OVERALL	66% $(\frac{176}{268})$	72% $(\frac{112}{155})$	68% $(\frac{288}{423})$

In our series, T₁N₁ lesions behave like T₂N₀ lesions. We will continue to monitor this relationship because of its prognostic importance.

Survival rates were not significantly different from the rates of control of disease for each stage. As would seem logical, control rates reflect survival, at least in this series.

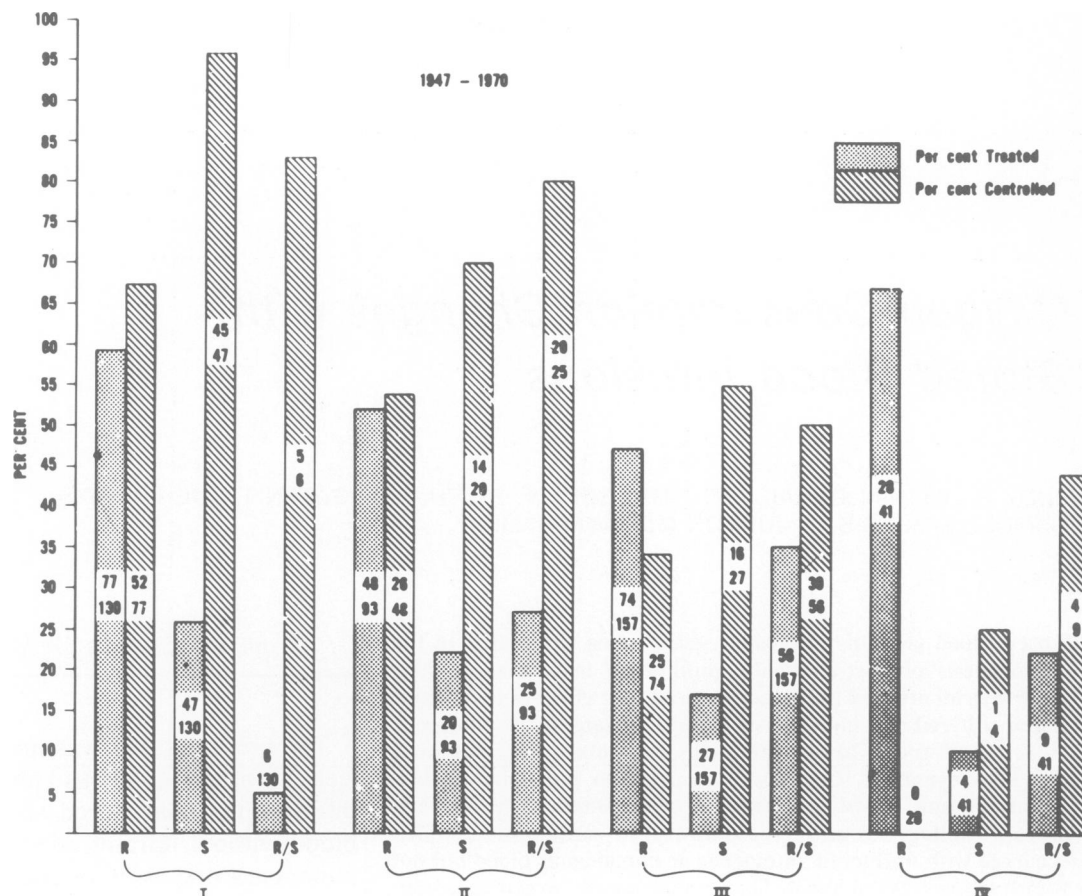
Unlike Fayos and Lampe,³ our results in Stages I and II were statistically significant in difference, and these stages could not be combined.

Overall, the T N M staging of the AJC has shown its merit in the rates of control and survival in our series of cases.

Finally, we join others in urging cooperative study for the treatment of carcinoma of the oral cavity and in cancer of the head and neck region, in general. Reports like ours are, 1) non-randomized, and, 2) small in number of cases so that much meaningful information cannot be retrieved for proper statistical analysis. Our results will always be suspect because of selection (non-randomization).

A number of questions arise from this review which have been asked before, to which answers will not be forthcoming until randomized cooperative studies are performed: 1) Does radiotherapy provide equivalent control of disease with surgery? In our series, it does, in the supravoltage era. 2) Does combined therapy provide better control of disease than single mode therapy? In our

FIG. 3. More cases were treated with radiotherapy but better control was obtained with surgery for each stage of disease in the entire period studied (1947-1970).



series, it does not, in the supervoltage era. 3) Is the T_1N_1 lesion more favorable than its Stage III indicates? In this review, it is.

Until such time as we have more meaningful data through cooperative studies, it would appear that treatment of carcinoma of the oral cavity will largely depend on the availability of a well-trained radiotherapist. In treatment facilities without experienced radiotherapists, surgery would appear to be the treatment mode. The availability of an experienced radiotherapist allows for the choice of either surgery or radiotherapy, taking into account the factors of preservation or loss of function, time and economy, while keeping control of disease and the welfare of the patient as the goal in treatment.

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